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EXAMINER	
FUBARA, BLESSING M	

ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/938,667	PETERSEN, JENS	
	Examiner	Art Unit	
	BLESSING M. FUBARA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *129-147* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *129-147* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/23/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of request for continued examination under 37 CFR 1.114, amendment, remarks, IDS and power of attorney, all filed 12/23/08. Claims 91-128 are canceled; new claims 129-147 are added and are pending.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/23/08 has been entered.

Response to Arguments

Previous rejections that are not reiterated herein are withdrawn.

The Claims :

Claim 129 is drawn to method of treating urinary incontinence, the method comprises injecting "hydrogel that comprises about 0.5 to 25% by weight based on the total weight of the hydrogel," with the hydrogel having complex viscosity of about 2-50 Pas and elasticity modulus

of about 1-200 Pa; the hydrogel contains less than 50 ppm monomeric units and the polymer is prepared by combining acrylamide and methylene bis-acrylamide.

The recitation that the polymer is "the product of a method … bis-acrylamide," is the process of preparing the acrylamide hydrogel. It also noted that no specific amount of the acrylamide is recited. "Less than 50 ppm monomeric units" in the hydrogel represent residual amounts of the starting acrylamide monomer and the cross-linker methylene bis-acrylamide. The viscosity and the elastic modulus are inherent properties of the hydrogel or properties that are intrinsic to the hydrogel.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 143 and 145 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejection. The recitation in claim 144 that the hydrogel is injected into the submucosa of the urethra is new since the original specification envisioned injecting the hydrogel "under the submucosal membrane of the urethra" and not into submucosa of the urethra (see paragraph [0041] of the published application. Applicant has indicated that paragraph

[0041] of the published application provides support for new claim 143. However, review of the specification at paragraph [0041] of the published application reveals that was envisioned at the time the original specification was filed is injection under the submucosa of the urethra and not into the submucosa of the urethra. For claim 145, paragraph [0032] envisions the hydrogel to contain cells and not that the injection step comprises introduction of cells.

Correction is respectfully requested.

5. Claims 129-147 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 129 recites the limitation "the product" in line 3. There is insufficient antecedent basis for this limitation in the claim. Product in line 3 is the first occurrence of the term.

7. Claim 141 recites two values of polyacrylamide in the same claim and it is unclear how there could be present two different amounts for the same acrylamide compound. Correction is respectfully requested.

8. Claim 145 is unclear because it is confusing how the step of injecting comprises introduction of cells. Correction is respectfully requested.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 129-147 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vogel et al. (US 6,335,028).

Vogel discloses method of treating urinary incontinence by administering, by injection into esophageal wall or via the urethra and into the wall of the bladder sphincter and urethral wall, acrylamide based hydrogel produced with about 25 to about 98% acrylic monomer such as methacrylamide and about 2-about 50% methylene bis-acrylamide and containing autologous cells (abstract; column 4, lines 31, 32, 51-67; column 6, lines 1-16;column 7, lines 7-10, 18, 21; column 10, lines 40-44; Examples 1 and 2); sterile and pyrogen free injectable solutions are employed for the storage of the hydrogel product (column 6, lines 58-60). Vogel specifically teaches that "the particles are implanted into appropriate tissue muscle or organ, etc. as a bulking agent" (column 4, lines 30-32) and the autologous cells incorporated in the hydrogel are obtained from the area where implantation is to be made (column 4, lines 46-38). Since the Vogel reference does not disclose the presence of residual monomeric units in the acrylamide hydrogel, and since the residual monomer in the product is expected to be very minimal if any, Vogel renders less than 50 ppm and 10 ppm monomeric unit obvious meeting the limitation in claim 129, 140, 141 for less than 50 and 10 ppm monomeric unit. Stress, reflex and urge incontinence are forms of urinary incontinence and stress incontinence is contemplated by Vogel (see column 2, lines 34 and 35) meeting claim 142. The mucosa is the lining of the urethra so that regarding claim 143, the submucosa is part of the urethra and claim 143 is met. Furthermore, 10, 2 and 6'clock are sections of the urethra as desired in claim 144 and the artisan has the technical knowledge of injecting the hydrogel into any of the sections of the urethra to achieve the

expected goal of reducing urinary incontinence, and absent unexpected result, injecting into any of the sections as stated by claim 144 is not inventive over the prior art.

Vogel discloses injectable acrylamide based hydrogel, and being injectable, the hydrogel would intrinsically have the viscosity that is characteristic of injectable hydrogels such as the claimed viscosities. The hydrogel contains cells (column 4, line 57) or other active agents (column 10, lines 54-67). The viscosity and modulus of elasticity recited in claims 129, 134, 138, 139 and 141 are properties of the hydrogel such that the viscosity and elasticity modulus requirements are met. Vogel contemplates reacting from about 25 to about 98% methacrylamide with bis acrylamide to form the hydrogel as described above. The injection of the hydrogel into the urethra as in claim 129 reads on Vogel's introduction of the hydrogel via the urethra (column 10, lines 41 and 42). With regards to claim 130, Vogel does not report the ratio of the acrylamide to bis-acrylamide in terms of molar ratios but reports %amount of acrylamide used to % amount of bis acrylamide, but the ordinary skilled artisan in the field of acrylamide gels knows how to calculate molar amounts of bis-acrylamide in relation to molar amounts of acrylamide needed to form the desired polyacrylamide gel having the desired consistency. Further, with regards to claims 132, 133 and 141 and the %amount of hydrogel, the artisan has the technical capability of using appropriate amounts of the hydrogel that would provide the anticipated relief from urinary incontinence. The requirement for pyrogen free environment in claims 135, 141 is met by Vogel's teaching of pyrogen free environment as a suspension medium (see 6, lines 56-59) with the large amount of the pyrogen free water in claim 135 representing amounts of the water that can be used at the discretion of the artisan for suspension of the gel and absent factual showing, the recited amount of the pyrogen free water

present in the hydrogel of the claims is not inventive over hydrogel of Vogel that is suspended in pyrogen free environment. The presence of cells in the hydrogel of Vogel meets claims 145 and 147 and stem cell of claim 146 is one of the forms of cell that is encompassed in a broad teaching of cells; allowing for cellular engraftment to the surrounding tissues derives from the characteristic of the cells such that the requirement is met when the hydrogel of Vogel containing cells is introduced via the urethra. The polymers of Vogel are cross-linked (column 6, line 11) meeting claim 137. Regarding claim 136, Vogel does not specifically teach the amount of the polymer in the hydrogel. But, the hydrogel of Vogel comprised of polyacrylamide, for example, contains amount of the polymer and the artisan is capable of determining an amount suitable for the anticipated purpose of treating urinary incontinence. Therefore, taking the teachings of Vogel, one having ordinary skill in the art at the time the invention was made would be motivated to use hydrogel composition having an amount of the polymer that would provide the expected reduction in incontinence.

Response to Arguments

11. Applicant's arguments filed 6/11/08 have been fully considered but they are not persuasive.

12. Applicant's has reintroduced the Rule 132 declarations by Diamond and Dmochowski that have been fully addressed in previous rejections and that response will be reproduced below for applicant.

13. Applicant argues that Vogel is directed to tissue bulking, but Vogel specifically teaches treating urinary incontinence and the injection of the acrylamide hydrogel into the urethra is a form of bulking.

14. Applicant argues that the skilled artisan would have no way of predicting the combination of physical properties that might render polyacrylamide suitable for treating urinary incontinence (UI). The examiner disagrees because viscosity and modulus of elasticity are properties of the hydrogel as pointed to by applicant and a hydrogel composition such as that of Vogel would have those properties; and also Vogel specifically uses acrylamide hydrogel compositions to treat urinary incontinence. Applicant's argument that Annis uses polyacrylamide to elevate the urethra is noted, but Annis is not used in the current rejections.

15. With respect to the certain combination of physical or rheological properties of rigidity, elasticity and viscosity that make the claimed hydrogel effective in treating urinary incontinence, it is noted that applicant has not factually shown that the hydrogel of Vogel cannot have those properties considering that Vogel specifically uses acrylamide hydrogel to treat urinary incontinence.

16. Claims 129-147 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pavlyk (US 5,798,096) in view of RU 2148957 or Vogel et al. (US 6,335,028).

17. The claimed method of treating urinary incontinence comprises injecting the claimed composition into the urethra.

Pavlyk discloses cross-linked polyacrylamide hydrogel (claims 109, 110 and 123) produced from acrylamide and methylene bis-acrylamide monomers and apyrogenic or pyrogen free water (abstract; Table 1) meeting the limitations of the acrylamide hydrogels and pyrogen

free water of the claims 129, 141, 135; the hydrogel is used as endoprosthesis by way of sterile injections into tissues by way of canals of the corporum cavernosum (column 1, lines 5-10; column 10, lines 37-56) meeting the requirements for injections. Pavlyk discloses that the hydrogel provides bulking (column 3, lines 17-18) meeting the characteristic and intended use of the composition of claim 129 that is injected into the urethra to treat urinary incontinence and the composition of Pavlyk would intrinsically impede flow of urine; the hydrogel of Pavlyk has low viscosity (column 2, lines 58-67) and the Pavlyk hydrogel would inherently have the viscosity and elasticity properties recited in claims 129, 134, 138, 139, 141. The amount of the acrylamide in the hydrogel ranges from 3.5 to 9.0% touching pints along the claimed acrylamide range of 0.5 to 25% as in the generic claims 129, 133, 141. The hydrogel of Pavlyk would intrinsically exhibit the intended use of the claimed hydrogel and would have the claimed properties since a product and its properties cannot be separated and thus meets claims 129, 134, 138 and 139. The 3.5% acrylamide of Pavlyk is less than 15%, 10%, 7.5%, 5% (meeting claims 129, 131-133, 141). The amount of water or aqueous solution in Pavlyk ranges from 88% to 96% (see Table 1) meeting the water limitation of at least 75% of claims 135 and 141 and Pavlyk's use of pyrogen free water meets the use of pyrogen free water in the claims 129, 135 and 141. Since the reaction between the acrylamide monomer and the methylene bis-acrylamide monomer cross-linking agent goes to completion, since the Pavlyk reference does not disclose the presence of residual monomeric units in the acrylamide hydrogel, and since the residual monomer in the product is expected to be very minimal if any, Pavlyk renders less than 50 or 10 ppm monomeric unit obvious as in claims 129, 140. 141. For claim 130, the artisan is

able to determine the ratio of the acrylamide to bis acrylamide that would produce the desired gel.

For claims 145 and 146, Vogel teaches including cells into the hydrogel and stem cell is a specific cell encompassed by generic disclosure of cells. For claim 147, it is the cells in the hydrogel that allows for cellular engraftment to the surrounding tissue so that when hydrogel containing cells is injected, claim 147 is met. Furthermore, 10, 2 and 6'clock are sections of the urethra as desired in claim 144 and the artisan has the technical knowledge of injecting the hydrogel into any of the sections of the urethra to achieve the expected goal of reducing urinary incontinence, and absent unexpected result, injecting into any of the sections as stated by claim 144 is not inventive over the prior art.

While Pavlyk discloses injecting the hydrogel into caverns, Pavlyk does not inject the hydrogel into the urethra. But RU reference 2,148,957 teaches that the polyacrylamide hydrogel, "a gel within the scope disclosed by Pavlyk" is injected into the ostium of the ureter to impede the flow of urine (see paragraph of remarks filed 2/27/06 and first full paragraph on page 10 of remarks filed 10/08/07). Furthermore, Vogel treats urinary incontinence by injecting polyacrylamide hydrogel into the urethra (column 10, lines 40-45). Regarding new claim 142, stress, reflex and urge incontinence are forms of urinary incontinence, and the submucosa is part of the urethra. Therefore, since treating urinary incontinence involves impeding flow of urine, taking the teachings of the Pavlyk, RU 2,148,957 and Vogel, one having ordinary skill in the art at the time the invention was made would have reasonable expectation of success that injecting the hydrogel of Pavlyk into the urethra as taught by Vogel would impede urine flow and reduce the likely hood of incontinence.

Response to Arguments

18. Applicant's arguments filed 12/23/08 have been fully considered but they are not persuasive.

19. Applicant argues that Pavlyk and RU 2148957 (Sknar) treat vesicoureteral reflux (VUR) while the invention treats urinary incontinence. The examiner agrees that Pavlyk and Sknar treat VUR. But, the rejection is not an anticipatory, and vesicouretic reflux occurs as a result of decreased resistance where urine refluxes back into the bladder. Therefore it would be reasonable to expect that administering polyacrylamide hydrogel into the urethra would successfully provide that resistance needed to impede urine flow.

Declarations under 37 CFR 1.132

The content of the previous response is reproduced below and since applicant mentioned these declarations that are the same declaration on record, the examiner has reproduced the response below for applicant.

20. David Diamond:

21. The declaration under 37 CFR 1.132 filed 6/11/08 is insufficient to overcome the rejection of claims 91-128 based upon 35 USC 103 over Pavlyk (US 5,798,096) in view of RU 2148957 and applicants admission (interview of 2/23/06 and remarks filed 2/27/06) and further in view of Annis et al. (US 4,857,041) as set forth in the last Office action because:

The Diamond declaration opines that the skilled artisan would not have at the time the invention was made presume or reasonably expect that using bulking agent to correct

vesicouretal reflux (VUR) would predictably be successful in treating pediatric urinary incontinence with "that bulking agent." The opinion declaration is not effective in overcoming the rejections because generic claims 91, 111 and 115-117 and the claim dependent therefrom are not directed to treating pediatric urinary incontinence. Furthermore, the suggestion by the RU, the Sknar reference, and acceptance by the declaration that, bulking agents have been used to treat VUR and other types of urinary incontinence in children provides a basis for the ordinary skilled artisan to reasonable expect that bulking agents injected into the tube connecting the urinary bladder to the outside would successfully bulk the tube and increase resistance to the flow of urine from the bladder to the outside.

22. Roger R. Dmochowski:

23. The declaration under 37 CFR 1.132 filed 6/11/08 is insufficient to overcome the rejection of claims 91-128 based upon 35 USC 103 over Pavlyk (US 5,798,096) in view of RU 2148957 and applicants admission (interview of 2/23/06 and remarks filed 2/27/06) and further in view of Annis et al. (US 4,857,041) as set forth in the last Office action because:

24. The declaration is of the opinion that the skilled artisan in the filed of Urology, knowing the differences between VUR and UI would not have been led by the teaching of the Sknar RU reference to treat UI with polyacrylamide hydrogel by administering the hydrogel to the urethra. However, the declaration appears to ignore the fact that the rejection of the claims is made over a combination of references and not just over the Sknar reference. The rejection is clear that Sknar is relied upon to show that polyacrylamide hydrogel impedes the flow of urine, the Sknar reference does not categorically say that the polyacrylamide hydrogel would only impede the flow of Urine from the ureter back to the kidneys. Since polyacrylamide hydrogel impedes flow

of urine when administered to the ureter, it is reasonable to expect that polyacrylamide hydrogel administered to the ureter would also successfully impede the flow of urine.

No claim is allowed.

Suggestion:

It was suggested to applicant, as was suggested previously and as stated on page 8 of applicant's remarks of 10/20/06, that the hydrogel be injected into the urethra at 0.5 cm distally from the neck of the bladder to overcome the art, explanation of why that position provides unusual and unexpected result may be necessary. Please note that Vogel injects hydrogel of the type claimed into the urethra.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BLESSING M. FUBARA whose telephone number is (571)272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Blessing M. Fubara/
Examiner, Art Unit 1618